

TB ISSUES & UPDATES

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NEW PROCESSES & PROCEDURES

REVISITING RATES OF TUBERCULOSIS REACTIVATION

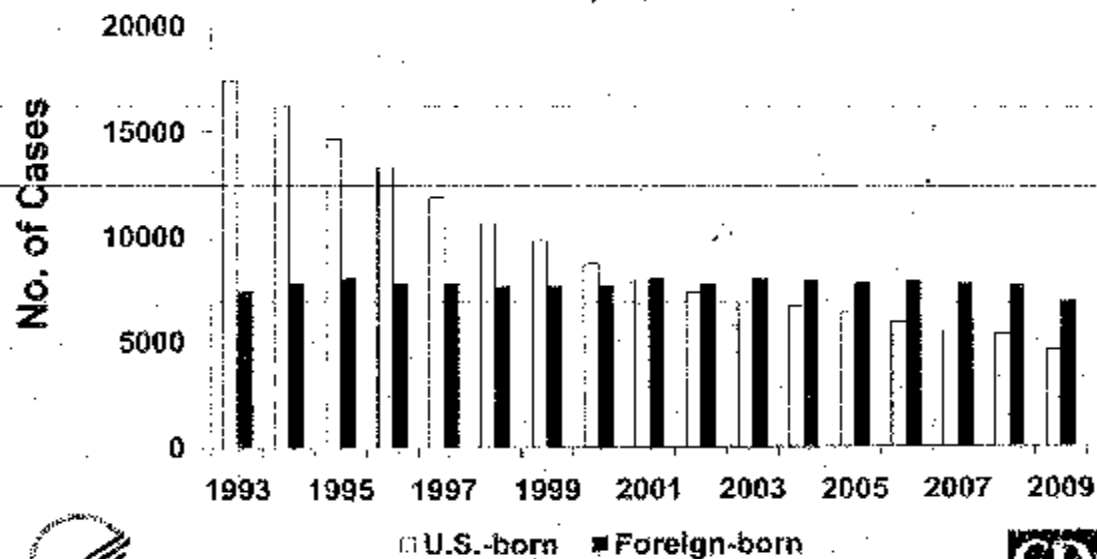
The rate of tuberculosis (TB) in persons with a positive tuberculin skin test in the United States is generally assumed to be 0.10 to 0.16 cases per 100 person-years. The rate, 0.40 to 0.058 per 100 person-years, was substantially lower than rates measured during the 1950s and 1960s. This decrease is likely due to the disappearance of old, healed but untreated TB in the U.S. population.

C. Robert Horsburgh, Jr., et al.

American Journal of Respiratory & Critical Care Medicine

Vol. 182, pp 420-425, 2010

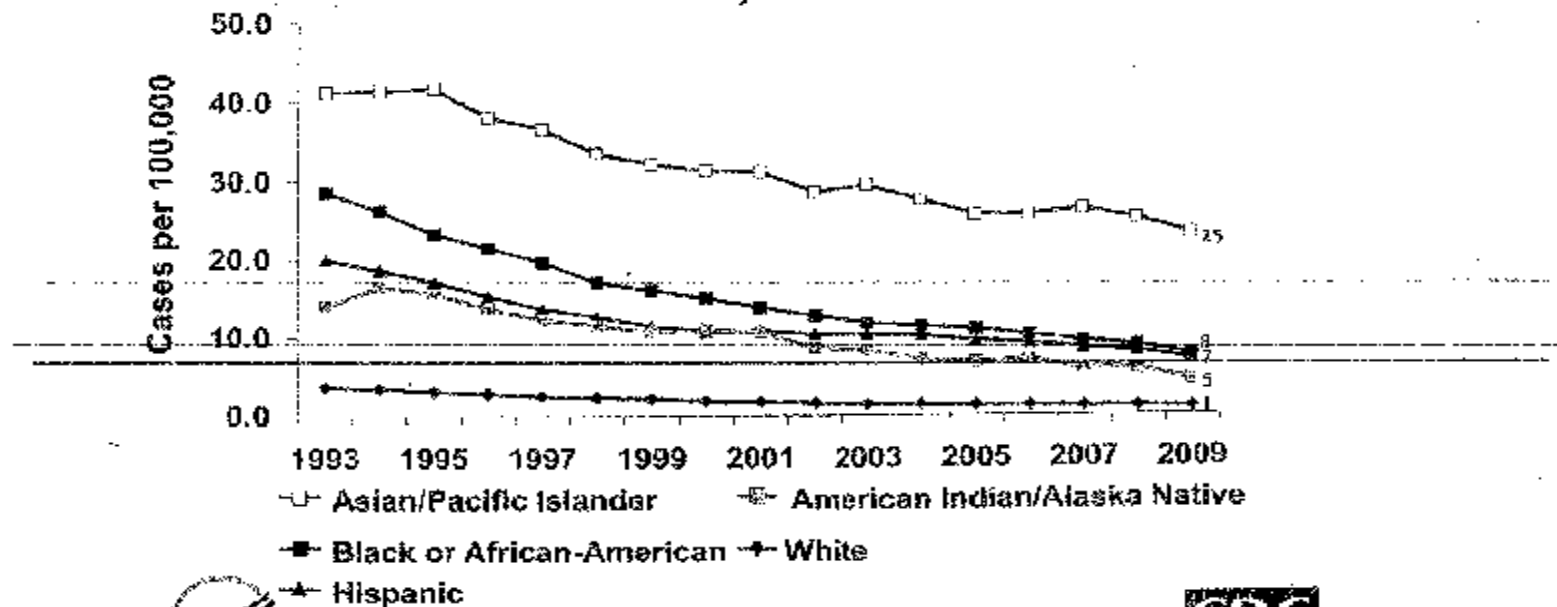
Number of TB Cases in U.S.-born vs. Foreign-born Persons United States, 1993–2009*



*Updated as of July 1, 2010.



TB Case Rates by Race/Ethnicity* United States, 1993–2009**



*All races are non-Hispanic. In 2003, Asian/Pacific Islander category includes persons who reported race as Asian only and/or Native Hawaiian or Other Pacific Islander only

**Updated as of July 1, 2010



Increased Group Risks for TB in U.S.

Revisiting Rates of Reactivation Tuberculosis

- American Indian/Eskimo x 5
- Hispanic x 7
- African-American x 8
- Asian x 25

MMWR, March 25, 2011. Incidence of TB in Ethnic Groups in the U.S. in 2010

WV PEOPLE QUICKFACTS

<u>PEOPLE</u>	<u>% in WV 2010</u>	<u>FACTOR OF SUSCEPTIBILITY</u>	<u>MINORITY INDEX</u>
White	93.9%		
Black	3.4%	8	27.2
American Indian/Alaskan Native	0.2%	5	1
	0.7%	25	17.5
Native Hawaiian/Other Pacific Islander	Z	25	0
Persons Reporting two or more races	1.5%		
Person of Hispanic/Latino origin	1.2%	7	8.4
White persons, not Hispanic	93.2%		
			TOTAL: 54.1

Factors Affecting TB Rates in WV

1. Minority Index

	TB Rank	Index
WV	46	54
HA	1	1340

2. AIDS

	TB Rank	AIDS Rate
WV	46	4.8
CA	2	10.2
MD	13	19.0

Factors Affecting TB Rates (cont.)

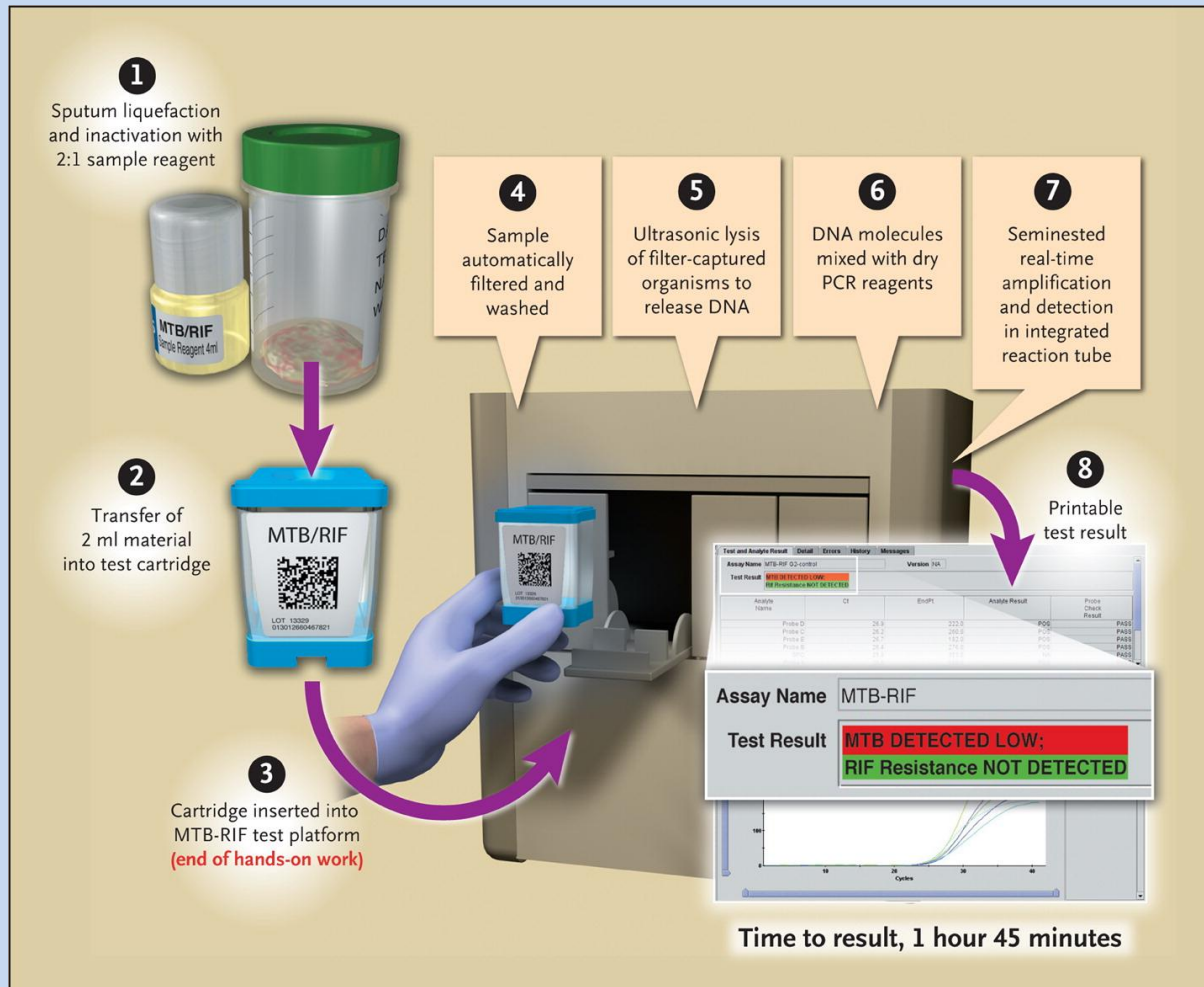
- 3. Diabetes - #1 Related to Obesity
- 4. Poverty Level - #5
- 5. Smoking - #1 or #2

Table. Comparison of 2010 and 2011 case counts and rates by state

<i>*data updated through 02/22/13</i>	2012 TB Cases	2011 TB Cases	2012 % of 2011 Cases	2012 Case Rate	2011 Case Rate	2011 / 2012 % change in cases	201 % cl ca
Alabama	134	161	83.2	2.779	3.352	-16.8	
Alaska	66	67	98.5	9.023	9.256	-1.5	
Arizona	211	220	95.9	3.220	3.402	-4.1	
Arkansas	70	85	82.4	2.374	2.893	-17.6	
California	2189	2323	94.2	5.754	6.164	-5.8	
Colorado	64	70	91.4	1.234	1.368	-8.6	
Connecticut	74	82	90.2	2.061	2.286	-9.8	
Delaware	28	21	133.3	3.053	2.312	33.3	
District of Columbia	37	56	66.1	5.851	9.047	-33.9	
Florida	679	754	90.1	3.515	3.951	-9.9	
Georgia	361	346	104.3	3.639	3.526	4.3	
Hawaii	117	123	95.1	8.403	8.925	-4.9	

North Dakota	26	7	371.4	3.716	1.022	271.4
Ohio	149	145	102.8	1.291	1.256	2.8
Oklahoma	88	94	93.6	2.307	2.484	-6.4
Oregon	61	74	82.4	1.564	1.913	-17.6
Pennsylvania	234	260	90.0	1.833	2.040	-10.0
Rhode Island	23	27	85.2	2.190	2.570	-14.8
South Carolina	122	140	87.1	2.583	2.996	-12.9
South Dakota	19	15	126.7	2.280	1.821	26.7
Tennessee	164	156	105.1	2.540	2.438	5.1
Texas	1233	1325	93.1	4.732	5.169	-6.9
Utah	37	34	108.8	1.296	1.208	8.8
Vermont	4	8	50.0	0.639	1.277	-50.0
Virginia	235	221	106.3	2.871	2.727	6.3
Washington	185	201	92.0	2.682	2.946	-8.0
West Virginia	8	13	61.5	0.431	0.701	-38.5
Wisconsin	71	70	101.4	1.240	1.226	1.4
Wyoming	3	4	75.0	0.520	0.705	-25.0

GeneXpert



UPDATE ON GENEXPERT DIAGNOSIS OF TB IN WV LAB

- All tests so far are producing great results compared to MTD. The GeneXpert procedure is much simpler than the MTD and results are produced much faster.
- OLS staff is excited to be able to use only the GeneXpert test soon.

IGRA (T-SPOT)

- Persons who are foreign born
- Persons who have had BCG vaccine
- Persons who are HIV infected
- Persons who are a known or suspect contact to an active case of TB that you believe would be at risk for follow-up to TST reading
- Persons with positive PPD without any known risk factors as ordered by TB Clinician

The only persons eligible for use of WVDTBE supplied testing material are listed above. Any TST or IGRA done outside the above stated parameters is the responsibility of the administering health department unless you have written approval for unique situations from WVDTBE personnel.

COMPARISON OF GAMMA INTERFERON AND TUBERCULIN SKIN TEST IN PREDICTING TUBERCULOSIS DEVELOPMENT

Interferon-Gold-Release Assay performed better than tuberculin skin test in predicting who in control group of those household contacts which refused prophylaxis would develop active tuberculosis.

Diel, R. et al. – AMJ Resp. Crit. Care Med 2011 Jan 1; 183:88. German study of contacts of Active tuberculosis cases

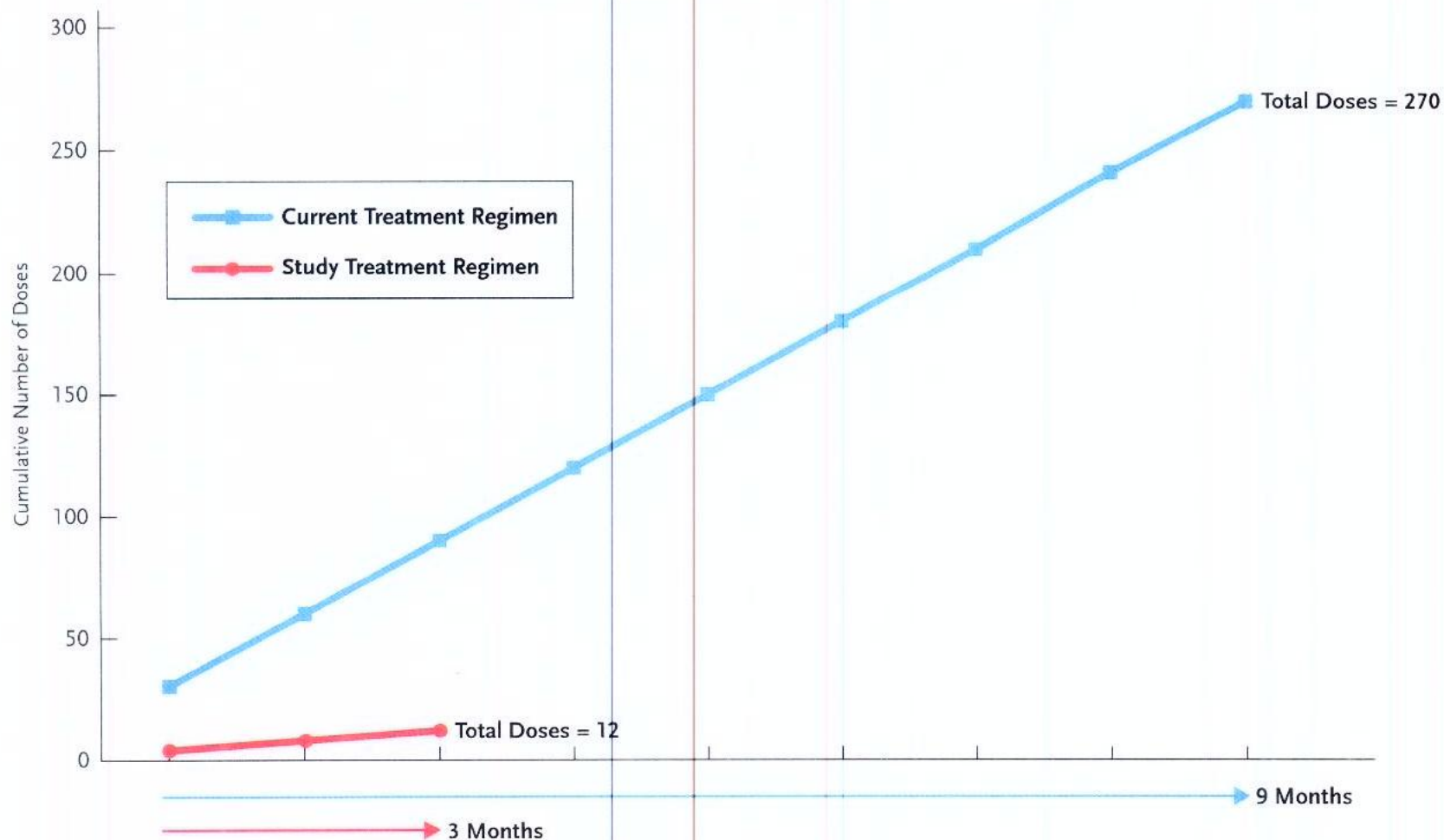
T-Spot outperformed tuberculin skin test in predicting which silicotic subjects that refused prophylaxis would develop tuberculosis.

Leung, C. C. et. al. – AMJ Resp. Crit. Care Med 2010; 182:834-840

SHORTENED COURSE OF TREATMENT OF LTBI

12-WEEK COURSE OF INH and RIFAPENTINE

Treatment of Latent TB Infection, Cumulative Doses Required, Current vs. Study Regimen



ASSESSING RISK FACTORS IN TUBERCULOSIS

Classifying Tuberculin Reaction

>5mm is classified as positive in:

- HIV positive persons
- Recent contact to TB case
- Fibrotic changes on CXR consistent with old healed TB
- Immunosuppressive disorders
- TNF α Antagonists

Classifying Tuberculin Reaction (cont.)

>10 mm is classified as positive in

- Recent arrivals from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children <4 years of age, or children and adolescents exposed to adults in high-risk categories

Medical Conditions Which Increase the Risk of Developing Clinical TB once TB Infection has Occurred:

• HIV infection	10-170
• Silicosis	2-30
• Abnormal chest radiograph showing fibrotic lesions	
• Diabetes mellitus	3
• Prolonged corticosteroid therapy	3
• Immunosuppressive therapy	
• Hematologic and reticuloendothelial diseases	10
• End-stage renal disease	2-16
• Intestinal bypass	30
• Post-gastrectomy	6
• Chronic malabsorption syndromes	
• Carcinomas of the oropharynx and upper gastrointestinal tract	
• Being 10 % or more below ideal body weight	2
• TNF antagonist	20-30
• Alcoholic intake	3-10

Classifying the Tuberculin Reaction (cont.)

>15 mm is classified as positive in:

- Persons with no known risk factors for TB

Targeted skin testing programs should only be conducted among high-risk groups

HIV

- Drives epidemic proportion of TB in certain countries (South Africa)
- TB occurs across wide spectrum of immunodeficiency, not only those with low CD4 counts
- Latent TB & HIV = TB occurrence of 10% per year! (In 10 years, **ALL** those with HIV & LTBI will progress to active TB).

HIV (cont.)

- Atypical pulmonary and disseminated TB common
- TB in HIV needs modification of treatment
- HAART treatment results in an immune reconstitution inflammatory syndrome



Diabetes Mellitus

- Increases risk of TB 5 or more fold in LTBI
- Glycemic control affects TB incidence
- Low BMI is an additional risk factor for tuberculosis
- TB impairs glucose control and may require insulin therapy (esp. in early TB disease)
- Results of TB treatment same as non diabetic

Silicosis

- WV Miners: 1910 300,000
 1955 30,000
 2013 13,000
- Miners, sandblasters, monument workers, gravel pit workers, glass workers
- Lifetime risk of TB ~ 3-5X TB risk
- Macrophage competition between TB bacilli and silica particle



ILO International Classification of
Radiographs of Pneumoconioses
 (revised 1980) 

PROFUSION

3/3

SHAPE-SIZE

q/q

Renal Failure

- 2-25X risk of TB
- Dosage modified in renal failure or on dialysis
(No change for INH, RIF or PAS)
- Toleration of meds may be affected by uremia

Aging

- Nursing Homes, Assisted Living, Chronic Care hospitals
- Co-morbid D.M. and renal disease
- More drug interactions
- Aging lymphocyte function
- Carries “old TB germs”; less resistant organisms
- Less positive TB skin test in disease

Steroids

- Tolerated at less than 10 mg per day
- Used in ocular, pericardial, meningeal and immune reconstitution syndrome
- Increased TB risk in treatment of collagen disease, diffuse lung disease and chronic lung disease
- Immunosuppression in transplant treatment due to LTBI and TB in transplanted organ
- Treat LTBI (>5mm) before transplant and if donor has any TB history

Malignancies

- Hematological, Hodgkin's and other lymphomas
- Affected by weight loss and concomitant steroid and chemotherapy
- Co-existent lung cancer in TB – suspect in bacterial response and lack of clinical and radiological response (weight loss, chest pain, hoarseness)
- Head & neck and gastric carcinoma – gastric acid /AFB control
- Jejunioileal bypass surgery – weight loss considered important- treat LTBI 9 months prior to elective surgery

Anti-Tumor Necrosis Factor Agents

- Certolizumab
 - Etanercept
 - Adalimumab
 - Infliximab
 - Golimumab
 - Tofacitinib
- Cimzia
Enbrel
Humira
Remicade
Simponi
Xeljanz

Anti-Tumor Necrosis Factor Agents (cont.)

- Used in rheumatoid arthritis, inflammatory bowel disease, psoriasis and rheumatoid spondylitis
- TNF α useful in containing AFB and granuloma formation
- Risk high for TB in this group (30%)
- Consider both CXR and skin test or IGRA
- Treat for LTBI 1-6 months prior to starting TNF α drugs
- -Mab's – worse than -cept

Epidemiological data indicate that greatest with the risk of active TB is Remicade

TB rates of 53.8/100,000 with Remicade and 28.3 with Embrel vs. US rate of 5/100,000 (Wallis, et al. Clin Inf Dis 2004; 39:1254-56)

Possible increased risk of reactivation of latent TB infection (LTBI) with Remicade than Embrel (Wolfe, Arthritis and Rheumatism 2004; 50: 372-379)

Risk of new infections progressing directly to active disease appears to be similar for both drugs. (Wallis, The Lancet 2008; 8: 601-611)

What does CDC recommend before starting?

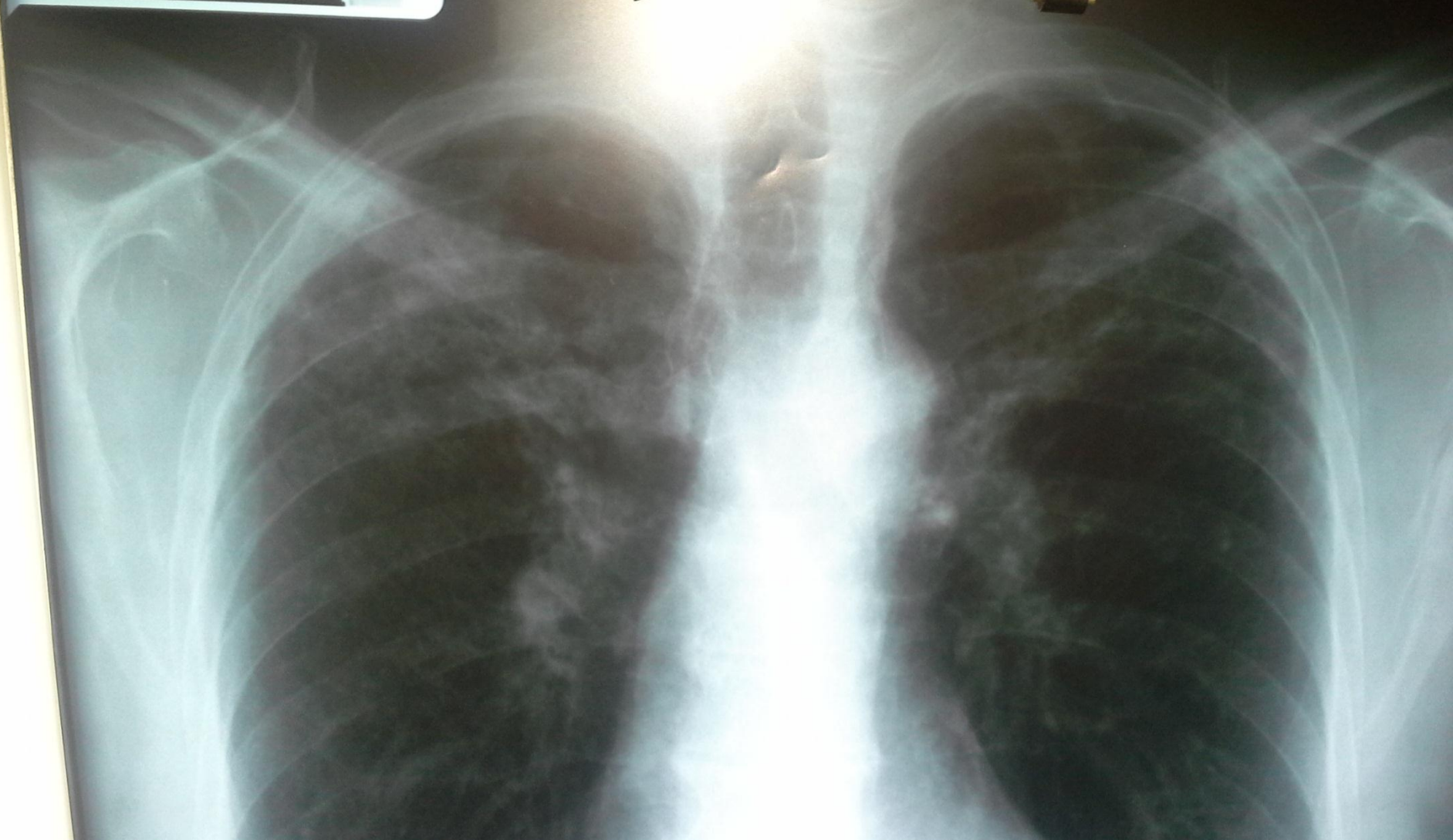
Screen for TB risk factors

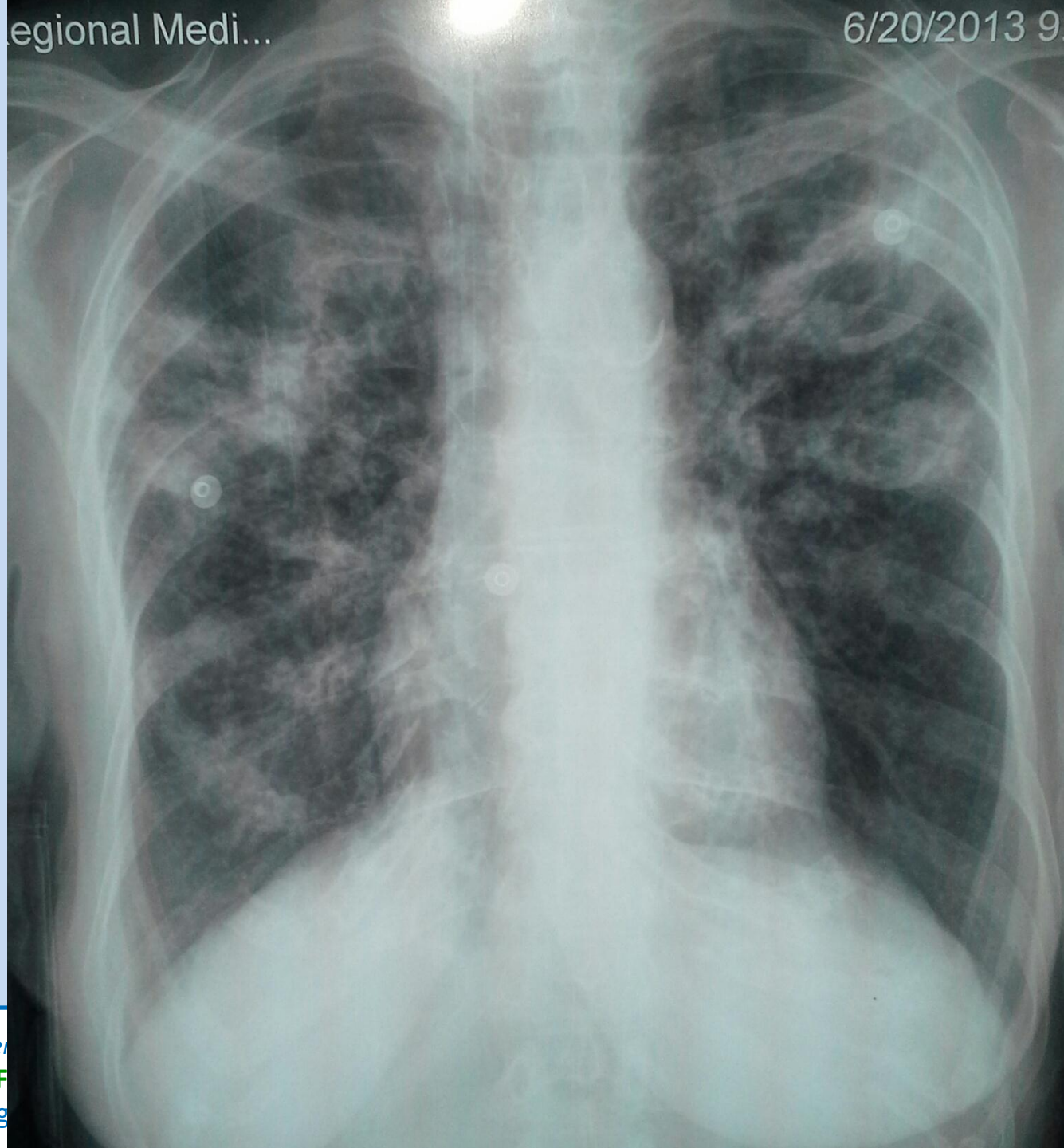
Test for LTBI and TB disease

Treat LTBI and TB disease according to published guidelines

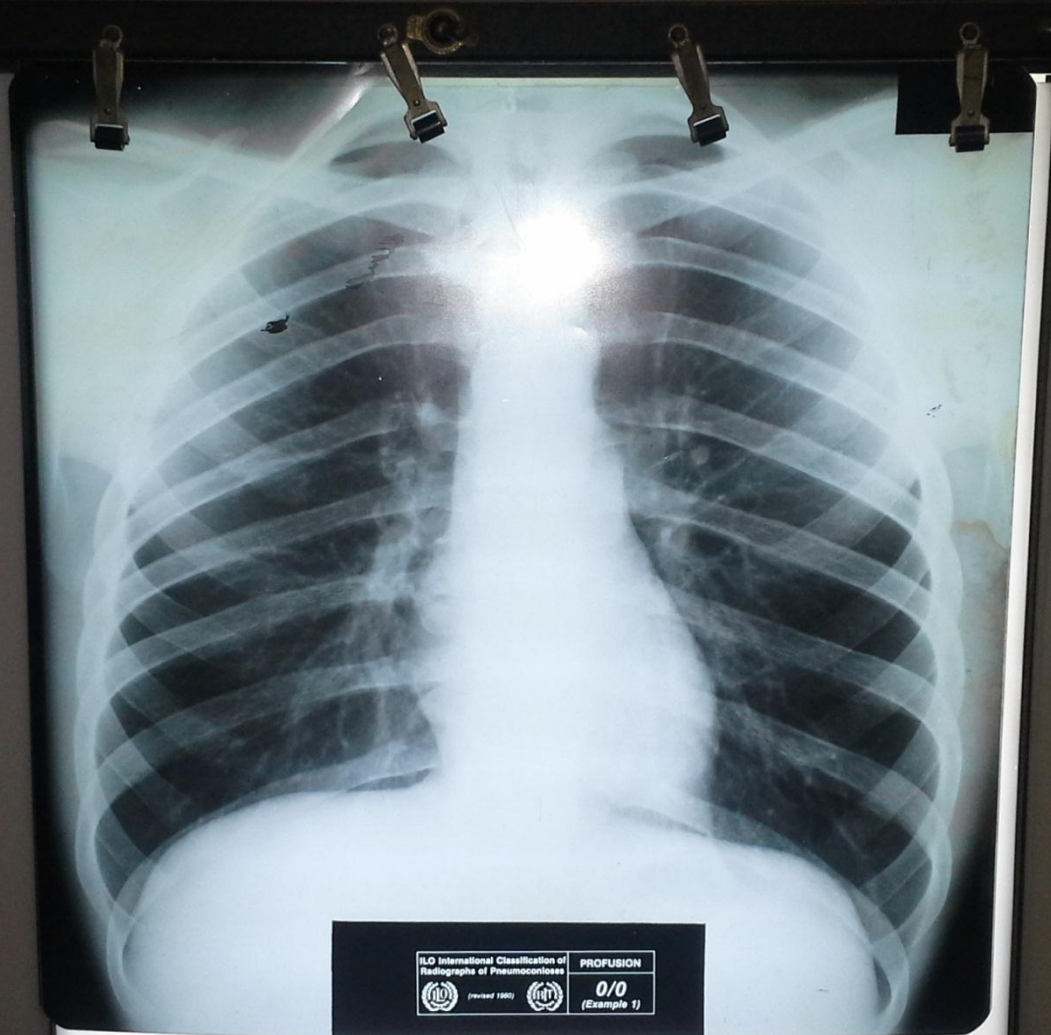
Treat those with TB risk factors for LTBI even if TST or IGRA negative

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Other Factors

- Abnormal CXRs showing fibrotic lesions
- Below 10% or more of IDEAL body weight
- Alcohol intake
- Smoking